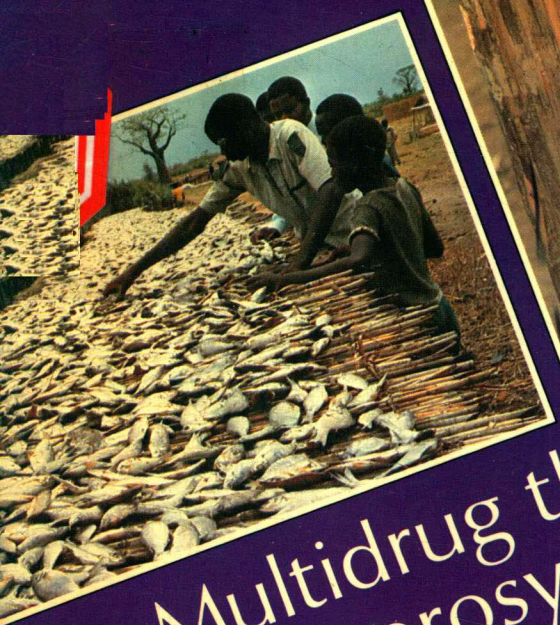
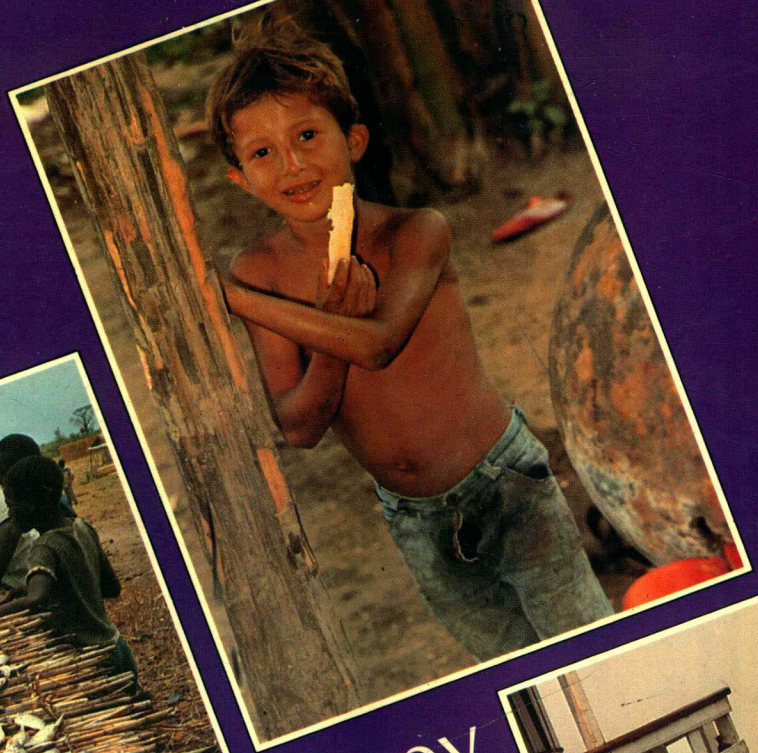
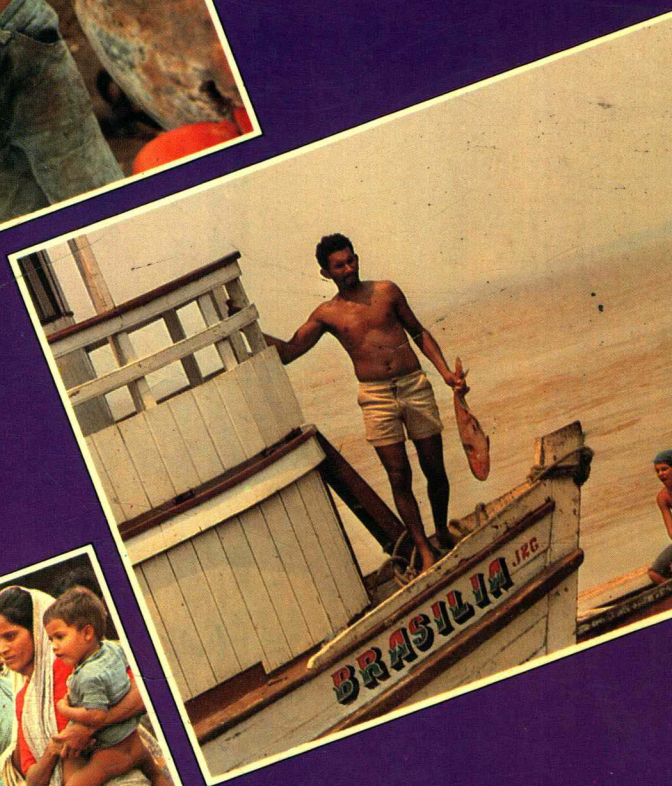
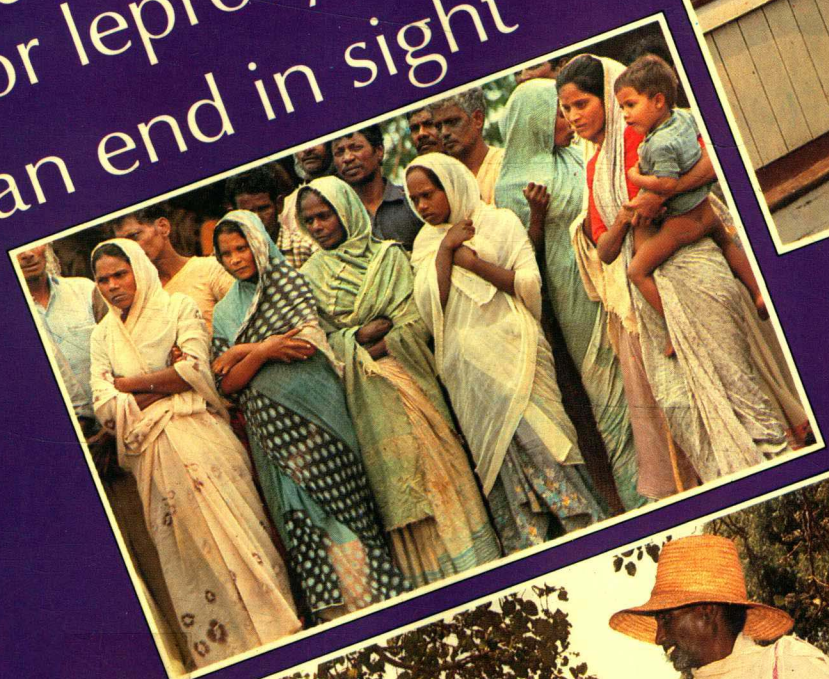






Multidrug therapy for leprosy: an end in sight



Multidrug therapy for leprosy: an end in sight

How five countries

INDIA

ETHIOPIA

MALAWI

VENEZUELA

BRAZIL

are using drugs of today to make leprosy a disease of yesterday

World Health Organization
Geneva
1988

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1988

The statistical information presented in this brochure is based on data available to the World Health Organization as of April 1988. Moreover, the designations employed and the presentation of the material in the brochure do not imply the expression of any opinion whatsoever on the part of the Secretariat of the World Health Organization concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimination of its frontiers or boundaries.

Preface

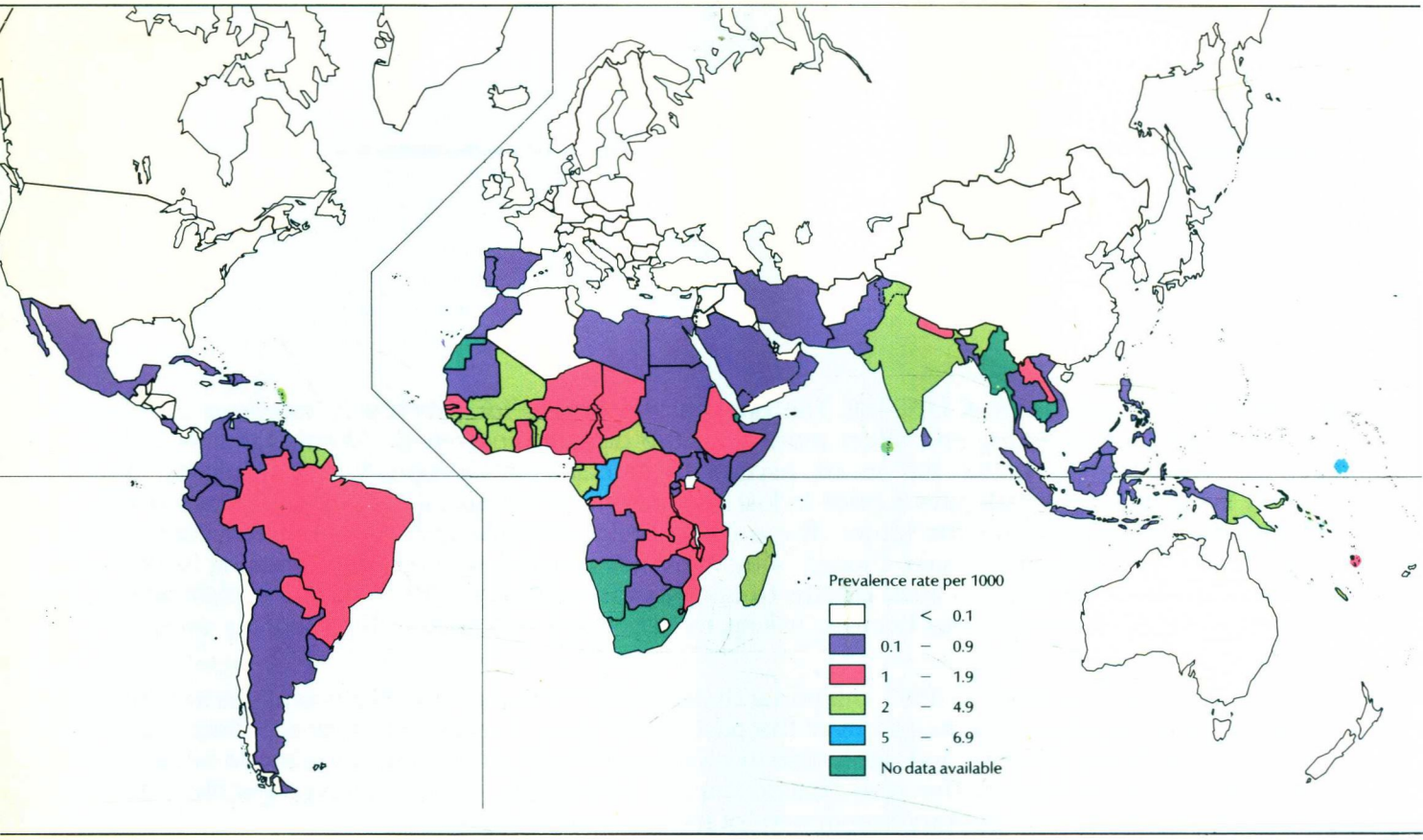
LEPROSY IS MORE THAN A DISEASE. The physical deformities for which it is notorious cause more than physical suffering and affect more than the diseased individual. Whole families and even communities live under the social, psychological pall cast by leprosy-related stigma. A country living under this pall pays a price in lost self-esteem, in lost social, cultural and economic productivity, in lost hope for the future. These costs are incalculable and in no way reflected in numbers of cases. They do explain, though, why countries afflicted with far more pressing health problems are prepared to go to great lengths to bring leprosy under control. They also explain why the international community has been so willing to help these countries in their leprosy control efforts.

First recommended by WHO in 1981, multidrug therapy (MDT) has introduced a new dimension to leprosy control. Experience of its use over the past seven years in over two million patients has shown it to be highly effective and applicable in a wide variety of geographic, socioeconomic and public health circumstances. This new disease control technology is here to stay. It is likely to remain for long the most important component of leprosy control strategy.

For the first time, thanks to MDT, leprosy can be seen not as a historical fatality but as a problem with a solution. There are probably still about eight to 10 million leprosy patients, however, who are not benefiting from this solution. The purpose of this brochure is to explain what MDT is, what it can do for leprosy control and why every effort should be made to extend its benefits to all communities with leprosy.

S.K. Noordeen

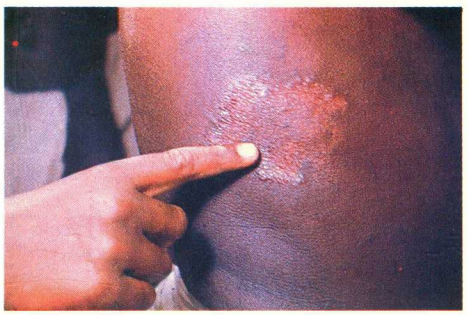
Chief Medical Officer, Leprosy
World Health Organization, Geneva



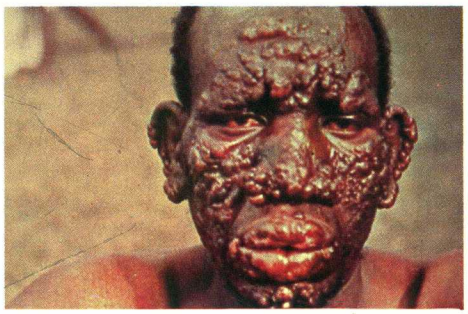
A world view of leprosy

Leprosy is believed to affect 10 to 12 million people in the world today. About a half are officially registered as leprosy patients. About a third have significant deformities. Only about a quarter are receiving regular treatment. South-East Asia, with 3.7 million cases, has 74% of the world's total. Of the 152 countries reporting leprosy cases, 53 are endemic for the disease (i.e., with at least 1 case per 1,000 inhabitants).

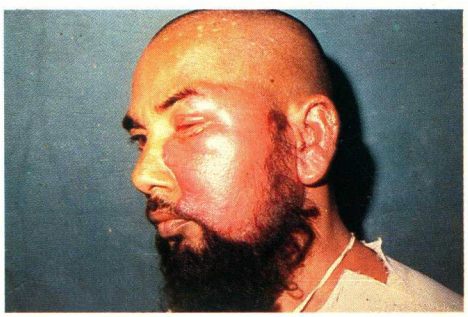
A leprosy primer



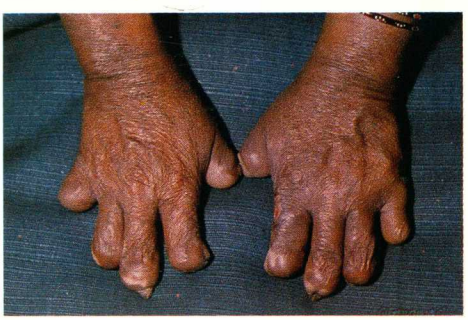
Paucibacillary (mild) leprosy



Multibacillary (severe) leprosy



Acute leprosy reaction



Leprosy-related deformity

Leprosy is a chronic disease caused by a bacterium, *Mycobacterium leprae,* known also as "the leprosy bacillus". *M. leprae,* which is closely related to the tuberculosis bacillus, was discovered in 1873 by the Norwegian physician, Armauer Hansen: hence the term "Hansen's disease" used in some parts of the world where the word "leprosy" is believed to carry overtones of social or religious condemnation.

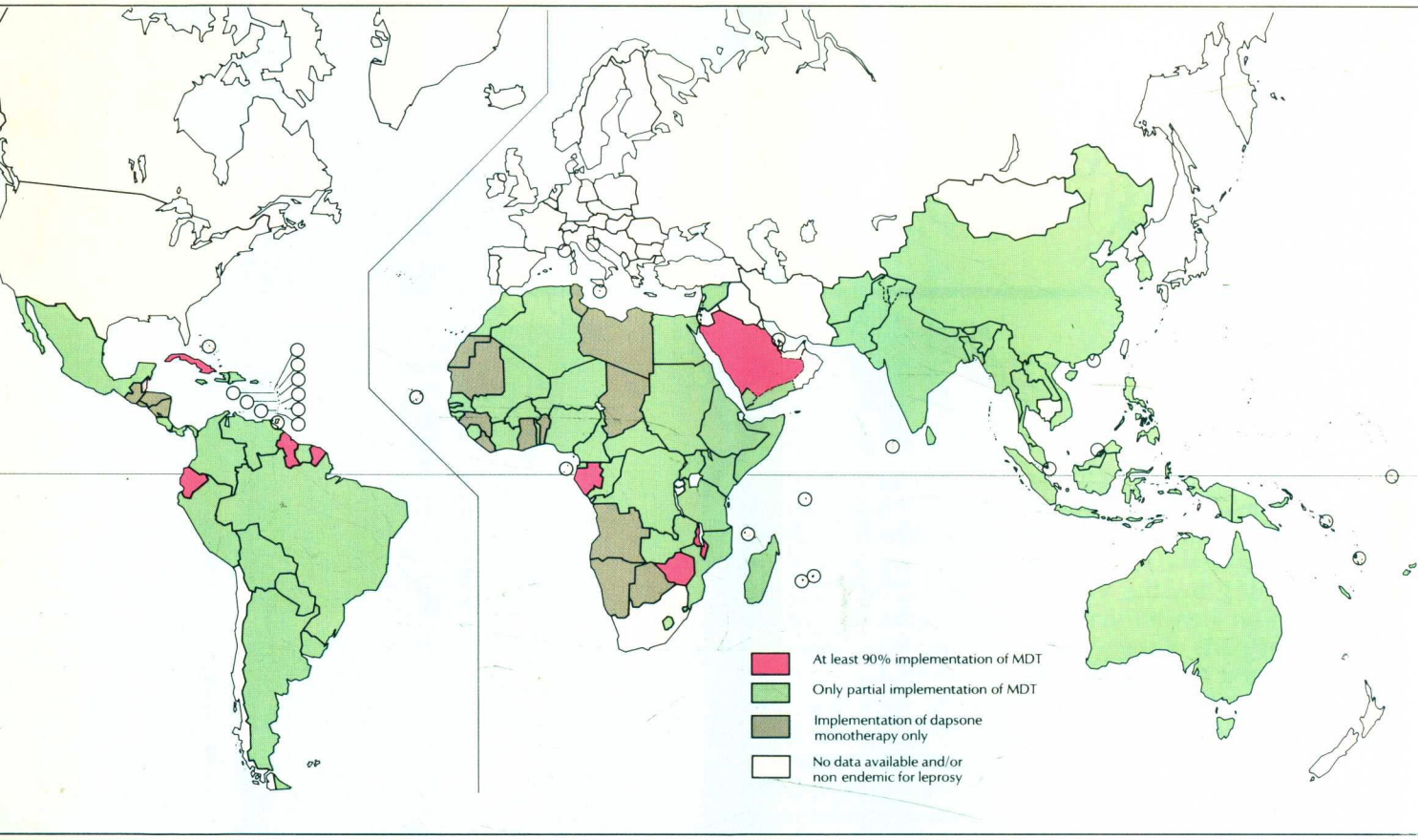
M. leprae is the slowest growing organism infectious to humans so far discovered. This partly explains why there may be a long interval — even 10 to 15 years — between initial invasion by the bacillus and the appearance of signs or symptoms of the disease.

The leprosy bacillus is believed to be transmitted from an infected to an uninfected person through the upper respiratory tract (breathed in as air-borne droplets) or through skin contact.

Fewer than 10% of people exposed to the bacillus actually develop leprosy: the lucky 90% or more are presumably capable of mounting a strong immune defence against the organism.

One or more numb (anaesthetic) white or reddish patches constitute the commonest sign of early or mild (paucibacillary) leprosy. Severe (multibacillary) leprosy is associated with one or more of the following: reddish patches; thickening and folding of the skin, particularly of the face and around the ears; nodules in many parts of the body; insensitivity to pain or temperature, resulting in neglected burn or contusion injuries and ulcers, particularly of the feet; nerve inflammation (neuritis) and tissue damage (resulting from the numbness) associated with typical deformities, ulceration and, ultimately, destruction of bone and other tissues.

Acute reactions or "flareups" with, in mild-to-moderate cases, inflammation of nerves and skin and painful nodules and, in more severe cases fever and general malaise may complicate the treatment of leprosy. In patients with the milder forms of the disease, reactions ("reversal reactions") may occur when natural immune defences against the leprosy bacillus are restored, possibly as a result of treatment. Severe reactions require urgent hospital treatment to prevent irreversible nerve damage and deformity.



A world view of multidrug therapy

By mid-1988, just over two million of the approximately five million registered leprosy patients in the 152 countries or territories reporting leprosy had been put on MDT and of these well over a quarter had completed their treatment and were no longer considered to have active leprosy.

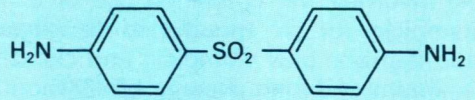
Multidrug therapy for radical leprosy control

LEPROSY has been a human scourge for five thousand years or more. For all but the last 40 or 50 years, the only strategy devised by humanity to control the disease was to isolate leprosy sufferers in leprosaria or socially hermetic colonies. The only "treatment" available consisted of folk remedies, like chaulmoogra oil, that provided occasional palliative benefit.

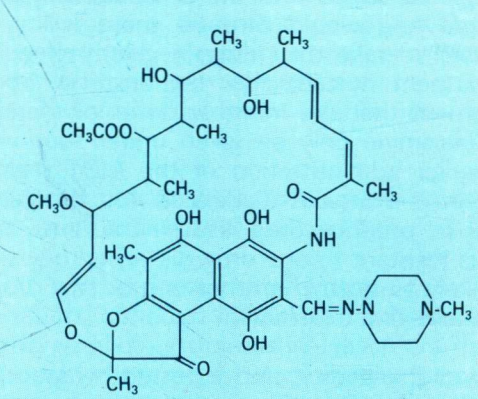
Dapsone, the first true antileprosy drug, was discovered in the early 1940s. Safe, inexpensive and effective — it kills 99% of bacilli within six months of a daily 50- to 100-mg dose — dapsone was hailed as "the final solution" to leprosy. It is, however, a relatively weak, slow-acting drug that has to be taken every day for long stretches of time — several years for paucibacillary leprosy, often for life for multibacillary leprosy. Without strict supervision, many patients do not take their dapsone treatment regularly enough, for long enough, to ensure cure of their disease.

Furthermore, a single drug used irregularly in too low doses or for too short periods not only fails to rid the body of an infecting organism. It also allows the organism to develop mutant strains resistant to the drug's effects. The result: relapse of patients initially cured by dapsone or failure of new patients to respond to the drug.

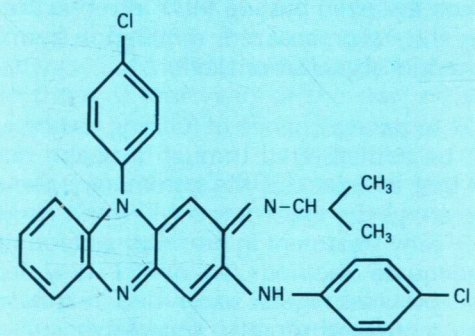
Studies conducted in the late 1970s under the auspices of the UNDP/WORLD BANK/WHO Special Programme for Research and Training in Tropical Diseases (TDR) disclosed resistant *M. leprae* in up to a third of cases in many endemic countries (in as many as 70% of cases in some areas). The world's only safe antileprosy drug seemed about to become useless. Urgent action was necessary.



Dapsone, a relatively slow-acting, weakly bactericidal drug, but inexpensive, safe and, if taken regularly, effective.



Rifampicin, an expensive but extremely powerful, fast-acting bactericidal drug: over 99% of leprosy bacilli are killed within a few days of a single 600-mg or 1500-mg dose. Can be toxic in some cases.



Clofazimine, a relatively expensive but safe dye with anti-inflammatory and weakly bactericidal properties. The skin darkening or discoloration it causes in some patients disappears when treatment is stopped.

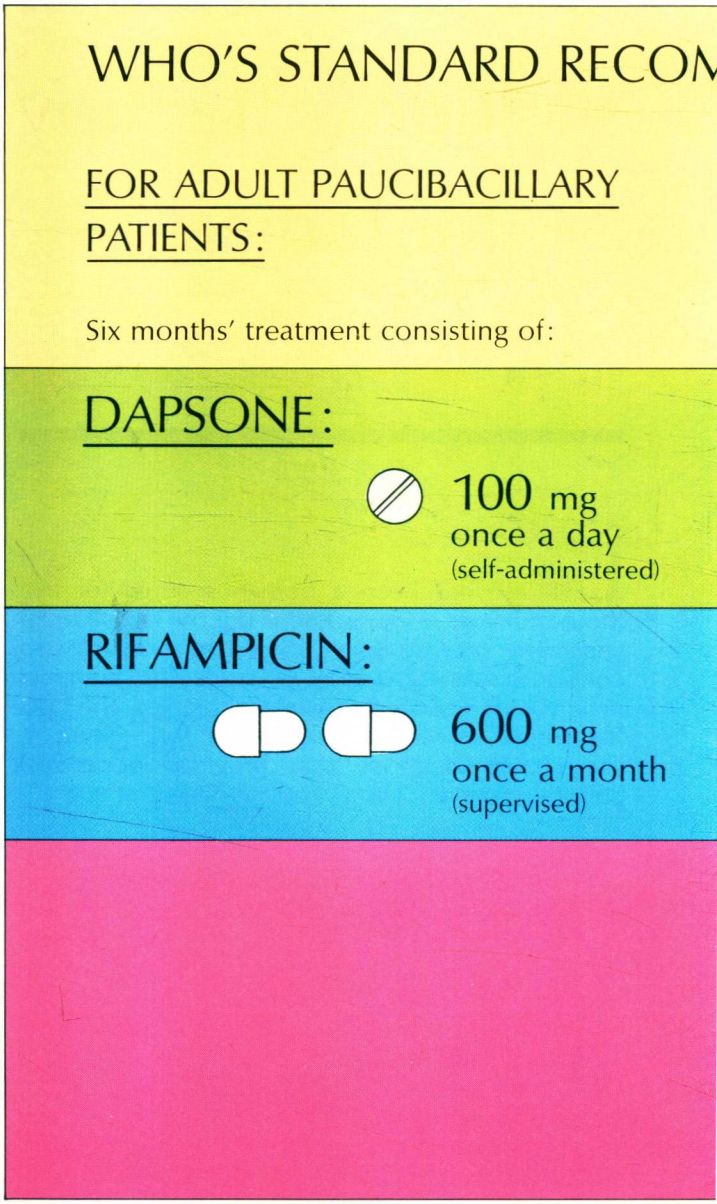
The three drugs used in WHO's standard multidrug therapy regimens.

Fortunately, since the early 1960s, about half a dozen different antileprosy drugs had been discovered. Two offered sufficient guarantees of safety, efficacy and ease of administration to be considered for large-scale use : rifampicin and clofazimine. Studies sponsored by TDR suggested that short, regular, intensive courses of treatment with a combination of these drugs plus dapsone itself would cure most patients of their disease, including those infected with dapsone-resistant leprosy bacilli, and that this treatment would not itself give rise to drug-resistant bacilli.

In 1981 a WHO Study Group devised a treatment schedule involving the combined use of dapsone plus rifampicin for six months in paucibacillary cases and dapsone plus rifampicin and clofazimine for a minimum of 24 (an average of 48) months in multibacillary cases: multidrug therapy (MDT) for leprosy was born. Patients, it was reasoned, would no longer be faced with the prospect of years of treatment and would thus be more willing and motivated to take their drugs regularly. Regularity of treatment would also be ensured by the requirement that the monthly doses of rifampicin and clofazimine only be given under supervision. The regular administration of the MDT regimens would in turn make it difficult for the leprosy bacillus to produce drug-resistant mutants, but if mutants resistant to one drug did arise, they would be unlikely to resist the other one or two drugs in the combination treatment.

Such was the theory, and it rested on laboratory research on the three drugs and on the encouraging preliminary results of a few field trials. But the growing threat posed by dapsone resistance argued against further delay. MDT had to be applied urgently. By the end of 1982, 15 countries had made a start in putting MDT into practice. The task, as they soon realized, required a formidable investment in organizational effort.

For MDT to have a chance of fulfilling its objectives, it must be administered through a health delivery system that (a) educates the community about the disease, about the existence of MDT and about the need for early treatment in preventing deformity, (b) uses adequate methods to detect new leprosy cases, (c) provides regular supervised treatment in a manner convenient and acceptable to most patients, (d) tracks down "irregular" (noncompliant) patients and (e) provides post-treatment supervision and care.



Creating such a system may be too much for a country burdened with economic and other health problems. Detailed national, district and community plans must be made. Manuals must be written setting out guidelines for the application of MDT — for the selection of suitable and the rejection of unsuitable patients for MDT, for the release of patients from treatment, for the diagnosis and treatment of patients with acute flare-ups or "reactions", and so on. Staff, medical and paramedical, must be trained in the diagnosis of leprosy and the dispensing of MDT. Laboratory facilities must be provided for bacteriological confirmation of "field" diagnosis and the monitoring of treatment progress. Treatment points and care clinics must be established at sites located more for the patients' than the control programme's convenience. Talks must be held with community leaders to brief them about the advantages of MDT and the need for their participation in setting up MDT treatment points and in encouraging patients to avail themselves of MDT. A transport and transport maintenance system must be set up to acquire and service the jeeps, motorbikes, bicycles, mules, or whatever means are used to bring MDT to patients. Accurate records must be kept of diagnosis, treatment, follow-up, drug supplies, etc. Inpatient facilities must be provided for patients with severe reactions. Resources must be provided for the care and the social and occupational

MENDED MDT REGIMENS

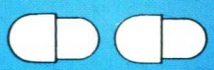
FOR ADULT MULTIBACILLARY PATIENTS:

At least 24 months' treatment, consisting of:

DAPSONE:

100 mg
once a day
(self-administered)

RIFAMPICIN:



600 mg
once a month
(supervised)

CLOFAZIMINE:

50 mg
once a day
(self-administered)

300 mg
once a month
(supervised)

rehabilitation of patients with physical deformities (as increasing numbers of patients with early disease are treated and discharged, patients with deformities due to late or otherwise inadequate treatment in pre-MDT days will gradually dominate the "residual" leprosy scene).

Is MDT worth it? Is the investment of time, effort and money required in setting up an MDT programme likely to pay off?

From the experience of the countries with MDT programmes — a sampling of five countries is described in the following pages — the answer is a resounding "yes"!

Among MDT's benefits:

- It is effective : early leprosy lesions — the characteristic anaesthetic, white or reddish patches — usually disappear within a few months of starting treatment or, in some cases, within a year or so of stopping treatment; patients with severe leprosy lose their infectivity to others within a few months of starting treatment and most can be discharged from treatment within two to four years.

- Relapses after stopping MDT have so far been rare — well under 1% of cases.

- MDT has been associated with very few severe side-effects, although in patients with anaemia or hepatic, renal or gastrointestinal disorders, the MDT drugs must either be avoided or administered with caution.

- MDT is finite: for the first time in the history of leprosy, patients can be told on starting treatment when they are likely to be taken off treatment (over 600,000 patients have in fact been released from treatment since 1982 — in some areas, the number of patients under treatment has dropped tenfold within three or four years of the start of an MDT programme).

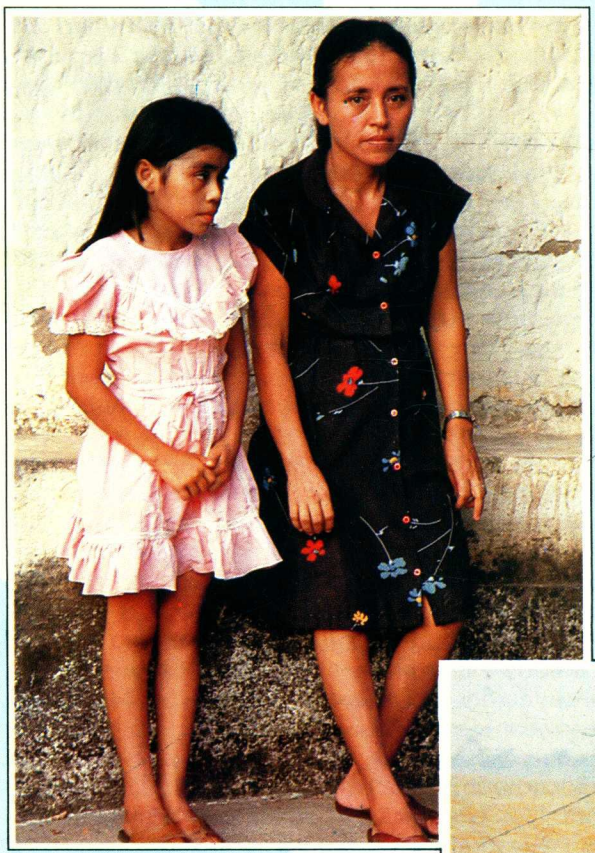
- Because it is finite, MDT makes it possible to speak of a "cure" for leprosy, provided patients take treatment regularly.

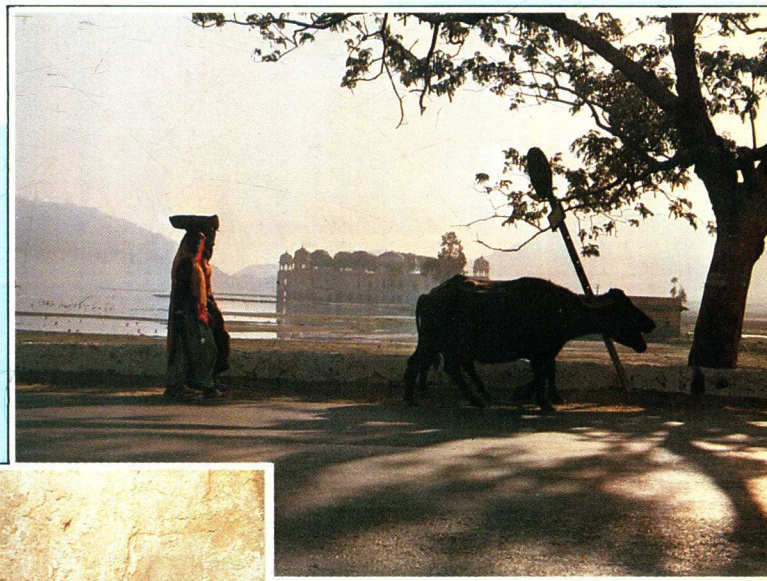
- Because it is effective, safe and finite, because it is easily accessible to patients, because it provides an opportunity for regular social contact and continuous care and supervision, MDT is welcomed by patients: 80 to 98% take their MDT pills regularly and patients are flocking for treatment wherever MDT programmes have been set up. As more and more people with suspected early lesions come for diagnosis and treatment, cases will probably be detected and treatment begun at an ever earlier stage, so that deformity — the consequence of delayed treatment — should become increasingly rare.

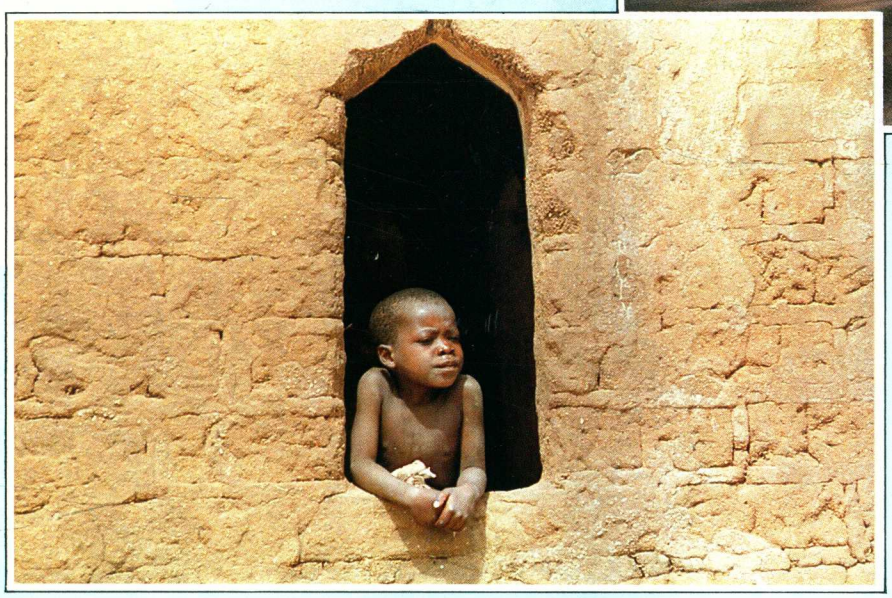
- MDT helps dispel social prejudices surrounding leprosy: patients can be treated "in the open" — at roadside treatment points, near markets, in bus stations, at primary health care centres — alongside patients with other diseases.

Multidrug therapy in action

a tale of five countries





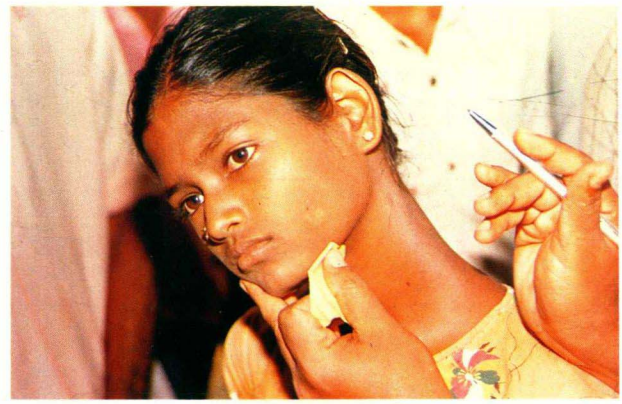


Multidrug therapy in INDIA

A NATIONWIDE attempt to deal with what is now recognized as "the foremost public health problem in India" began in 1955 with the launching of India's National Leprosy Control Programme. In 1983, encouraged by the advent of MDT, the Government decided to wipe out the disease, and the programme became the National Leprosy Eradication Programme (NLEP).

India, with an estimated four million cases of leprosy, has about one third of the world's leprosy population (vs. a sixth of the world's overall population). In 1951, when the first case records became available, there were an estimated 1.4 million leprosy patients and a prevalence rate of 3.8 cases per 1,000 population. As more cases were discovered, the figure rose steadily, decade by decade, to a peak of 3.9 million estimated (2.4 million registered) cases by 1981, when MDT was first introduced into a few districts. Since then, every year an average of 400,000 to 500,000 new cases have been detected and, thanks largely to MDT, about the same number discharged, bringing the total number of registered cases to 3.15 million by the end of 1987. With 1.4 million (41%) of these cases under MDT, India has the largest MDT programme in the world.

In parts of India, patients like this young woman who only have a single white patch, are told they have a skin infection that will clear up within a few months, thanks to MDT. Most early patches, like this one, clear up within six months of starting MDT. In some patients, patches remain after the statutory six-month MDT regimen for mild (paucibacillary) cases. They are inactive lesions containing no live leprosy bacilli, although the patient may think they indicate persistence of disease. In most cases, they disappear within 12 to 24 months after stopping MDT.



The NLEP is a monolithic institution run very much like an army. Plans, decisions, targets and guidelines issued by the top administrative bodies in New Delhi filter down through the different echelons of state and district leprosy officers to the 18,000 health workers, who cycle or walk from village to village encouraging patients to come to the roadside treatment points to receive their MDT pills every month. Records of treatment, of new cases, of follow-up examinations and of other operational details permeate back up to national headquarters, where more plans, decisions and targets are made or existing plans modified on the strength of the incoming data.

Three districts in the southern state of Andhra Pradesh illustrate how this massive MDT programme is being used in an apparently successful attempt to wipe out the disease:

Surgery to ensure partial closure of the eyelids could prevent blindness in patients such as this cycle rickshaw puller. Despite 20 years on dapsone therapy, he has developed lagophthalmos, an inability to close the eyelids caused by leprosy-induced damage to the facial nerve. Blindness commonly results from drying and ulceration of the cornea. Early MDT treatment can prevent such disabilities.

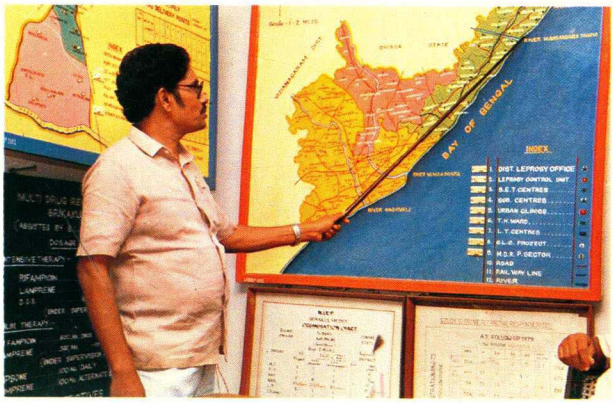
Srikakulam was one of the first districts in which MDT was introduced (in February 1983). There were 30,740 cases at that time and a prevalence rate of 19.1 cases per 1,000 population (one of the highest in the country). Four-and-a-half years later, by the end of 1987, only 4,311 cases (2.3 per 1,000) were left (equivalent to a drop in the world's total registered cases from five million to 700,000.)

In nearby Visakhapatnam district, MDT was begun in October 1985 and has released an average of over 8,000 patients a year from treatment vs. just over 3,000 a year before the introduction of MDT.

Further southwards on the Bay of Bengal coast, East Godavari district has just completed its pre-MDT screening or "weeding-out" period : careful examination of all 41,000 registered patients in the district made it possible to drop 12,000 inactive cases from the registers, bringing the prevalence rate down from 13 to 9 cases per 1,000 population in six months simply as an operational "spin-off" of MDT, i.e., without a single MDT pill being administered!

By the end of 1987, 73 districts had begun MDT. India aims by 1990 to set up MDT programmes in all 76 of the country's high prevalence districts, by 1995 in the remaining 125 moderately endemic districts and by 2000 throughout the entire country. If the initial results are sustained over the next decades — current annual relapse rates are generally under 0.1% (vs. about 2% for dapsone therapy) — optimism about the chances of bringing leprosy under control is justified. If and when the leprosy case-load falls to around 500 cases in a district, leprosy control could be handled by the country's primary health care system. A specialized or "vertical" programme as costly and cumbersome as the NLEP would no longer be needed and its funding and trained staff could be used for other purposes.

Meanwhile, patients released from treatment in MDT districts are registered as "CCCC" (chemotherapy completed, care continues) and are kept under regular six-monthly surveillance for any recurring problems, reactions or flare-ups of their disease.This surveillance period lasts two years for mild (paucibacillary) cases and five years for more severe (multibacillary) cases. A "care of the cured" period follows surveillance, during which NLEP staff help patients find work and return as fully-fledged members of the community.



Dr B. Raja Rao, District Leprosy Officer for Srikakulam District in the state of Andhra Pradesh, traces the district's MDT roadside treatment delivery points. Villagers from nearby communities, forewarned of the exact time of treatment by domiciliary visits from paramedical workers, gather at these points to receive their monthly antileprosy pills.

A woman leprosy patient from a tribal hilly area of East Godavari District on India's leprosy-endemic eastern seaboard proudly displays her "MDT child". When she saw how quickly her white leprosy patches disappeared after she started taking MDT, she refused to stop treatment when she became pregnant.